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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/040,103	03/17/1998	JAMES M. MASON	52494-21	1415

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EXAMINER
GUZO, DAVID

ART UNIT	PAPER NUMBER
1636	27

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/040,103	Applicant(s) MASON, JAMES M.	
	Examiner David Guzo	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8-11,13-40 and 42-70* is/are pending in the application.

4a) Of the above claim(s) *22-35,39 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,8-11,13-21,42-46,49-51,54-61 and 64-70* is/are rejected.

7)☒ Claim(s) *47,48,52,53,62 and 63* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). 26 .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 22-35 and 39-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 20-21, 46, 49, 51, 54, 55, 61, 64, 66-67 are rejected under 35 U.S.C. 102(e) as being anticipated by Pensiero et al.

Applicant claims methods for producing stable packaging cell lines for generation of human serum-resistant retroviral particles (RVPs) comprising introducing one or more packaging vectors into a human serum-resistant non-primate mammalian cell line wherein said vectors express a cellular targeting protein (such as env or VSV G protein,

etc.), gag and pol sequences sufficient to package the particle and collecting said cell line. Applicant also claims a method of producing stable retroviral producer cells comprising introducing a retroviral vector in the aforementioned packaging cell line and methods for producing RVPs comprising culturing the claimed producer cells. Applicant also claims producer cells and retroviral vectors produced by the claimed methods.

Pensiero et al. (U.S. Patent 6,329199, issued 12/11/01, effective filing date of 8/17/94, see whole document, particularly the Abstract, columns 3-7, paragraph bridging columns 9-10, etc.) teach a method for producing stable packaging and producer cell lines for generation of RVPs comprising introducing one or more packaging vectors into a human serum resistant non-primate mammalian cell line (Mv-1-Lu cells) wherein said vectors express a cellular targeting protein (such as VSV G envelope protein), gag and pol sequences sufficient to package the RVP and collecting said cell line. Pensiero et al. also discloses introducing a retroviral vector into the packaging cell line in order to generate a producer cell line and RVPs produced from the producer cell. With regard to the retroviral vectors which are produced by a different method but are claimed in a product by process context (Claims 20-21), even though the claimed retroviral vectors were produced by a different method, it must be considered that absent evidence to the contrary, said retroviral vectors are not patentably distinct from those disclosed by Pensiero et al. (See MPEP 2113). Pensiero et al. therefore teaches the claimed invention.

Claims 46, 49-51, 54, 55, 61, 64-70 are rejected under 35 U.S.C. 102(e) as being anticipated by Rother et al.

Applicant and Rother et al. (previously cited by the examiner, see whole article, particularly columns 15, 21 and Examples 1-7) recite the same methods of preparing stable retroviral packaging (and producer) cell lines for the generation of RVPs, said method comprising introducing one or more packaging vectors into a human serum resistant non-primate mammalian cell line (i.e. BHK cells) so as to express the retroviral genes (including a gene encoding an env targeting protein) necessary to package an introduced retroviral vector into said RVPs and packaging (and producer) cell lines produced by this method. Applicant and Rother et al. also disclose the same method for producing RVPs comprising culturing the producer cells, and methods for transferring heterologous genes to human cells (including brain cells) in vitro or in vivo comprising contacting the producer cells with the human target cells so as to release the RVPs to infect the target cells. With regard to the titers of viral particles produced, these titers are within the normal titers produced from standard retroviral producer cells known in the art and would be expected (absent evidence to the contrary) from those recited by Rother et al. Rother et al. therefore teaches the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 68-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pensiero et al. in view of Rollins et al.

Applicant claims a method of transferring a heterologous gene to human cells comprising contacting the claimed RVP producer cells with the target human cells (in vitro or in vivo) under conditions whereby the producer cells release the RVPs and thereby introduce the heterologous gene into the human cells.

Pensiero et al. is recited as in the above 35 USC 102(e) rejection of claims 20-21, 46, 49, 51, 54, 55, 61, 64 and 66-67. Pensiero et al. teach the generation of human serum resistant RVPs and the desirability of using these RVPs as vectors for transferring genes into human cells. Pensiero et al. does not teach contacting the RVP producer cells with the human cells to be transfected.

Rollins et al. (Cited by applicants, Human Gene Therapy, Vol. 7, 1996, pp. 619-626, see whole article, particularly the Abstract, p. 624) teaches use of retroviral producer cells to deliver gene to target cells in vivo, recites that a serious drawback to gene therapy using implantation of retroviral producer cells in human tumors is the human serum mediated destruction of these cells and teaches that use of serum resistant retroviral producer cells is required for effective production of vector particles in vivo.

The ordinary skilled artisan, seeking to develop a method for transferring genes to target human cells in vivo would have been motivated to use the human serum resistant RVP producer cells disclosed by Pensiero et al. in a method for introducing

heterologous genes into target human cells in vivo comprising contacting the target cells with the producer cells (as disclosed by Rollins et al.) because the RVPs disclosed by Pensiero et al. are designed to be delivered to human cells in vivo and because contacting human target cells with retroviral producer cells was a well known prior art method of delivering retroviral vectors to target cells in humans. It would have been obvious for the ordinary skilled artisan to do this because Rollins et al. teaches that cells lines which are resistant to lysis by human serum are a significant improvement in delivering retroviral vectors to target cells in humans. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 70 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pensiero et al. in view of Rollins et al. as applied to claims 68-69 above, and further in view of Culver et al.

Pensiero et al. and Rollins et al. are applied as above. Neither reference teaches implanting RVP producer cells in the human brain.

Culver et al. (Cited by applicant, Science, Vol. 256, 1992, pp. 1550-1552, see whole article, particularly the Abstract and p. 1552) recites the use of implanted retroviral producer cells to deliver a heterologous gene to target tumor cells in the rat brain and recites that this protocol can be used to treat tumors of the human brain.

The ordinary skilled artisan, seeking to develop a method for delivering retroviral vectors to the human brain would have been motivated to combine the teachings of Pensiero et al. on the generation of human serum resistant RVP producer cell lines (designed for human in vivo use) with the teachings of Rollins et al. and Culver et al. on the desirability of using human serum resistant retroviral producer cells for delivering genes to target human cells (in the brain) in order to implant the human serum resistant RVP producer cells in the human brain so as to deliver a heterologous gene to target cells in the human brain. It would have been obvious for the ordinary skilled artisan to implant the human serum resistant RVP producer cells disclosed by Pensiero et al. in the human brain so as to deliver a gene of interest to target human cells because Rollins et al. and Culver et al. teach the desirability of using human serum resistant retroviral producer cells to deliver genes to target cells in humans in vivo and because the use of implanted retroviral producer cells had been a well known technique to deliver retroviral vectors to target cells in vivo. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-6, 8-11, 13-21, 36-38, 42-45, 56-60 and 66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The newly added (in the amendment filed 2/26/02) limitation in claim 1 reciting that "...the non-primate mammalian cell line is not BHK." is not supported by the specification as filed. No support for specifically excluding BHK cells from the cell lines that could be used to prepare the recited retroviral packaging cell lines can be found. This is a NEW MATTER rejection.

Claims 58 and 63 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 58 and 63 recite the limitation of "...wherein the cell line exhibits no specific hybridization to a Moloney-MLV retrovirus gag-pol or env probe"; however, this limitation is present in the claims from which they depend. Therefore claims 58 and 63 do not further limit the claims from which they depend.

Claims 47-48, 52-53 and 62-63 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Faxes can be sent directly to the examiner at (703) 746-5061.

Any inquiry of a general nature or relating to the status of this application or proceeding or relating to attachments to this Office Action should be directed to Patent Analyst Zeta Adams whose telephone number is (703) 305-3291.

David Guzo
May 19, 2002

DAVID GUZO
PRIMARY EXAMINER
David Guzo